Haemophilus Influenzae
Invasive Disease (under age 5 years)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To correctly identify the serotype of invasive *Haemophilus influenzae* organisms in children under 5 years old.
2. To monitor the effectiveness of immunization programs and vaccines and to assess progress toward elimination of *H. influenzae* serotype B (Hib).
3. To identify children exposed to Hib cases and closely observe them for signs of illness.
4. To recommend antibiotic prophylaxis and/or immunization to appropriate contacts of Hib cases.
5. To identify additional cases and establish risk factors for non-Hib cases.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction; only cases under 5 years old are reportable**
2. Hospitals: **immediately notifiable to local health jurisdiction; only cases under 5 years old are reportable**
3. Laboratories: no legal requirements for reporting (see Section C2 below)
4. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin investigation on the same day as notification.
2. Contact laboratories as soon as possible after a case is reported and request that the *H. influenzae* isolate be submitted to Public Health Laboratories for serotyping.

   Note: Although laboratories are not currently required by law to submit specimens, the need to correctly identify the serotype of *H. influenzae* isolates from children under 5 years old with invasive disease has increased because Hib has become a rare disease.
3. Identify close contacts of patients with Hib and recommend antibiotic prophylaxis as appropriate within 24 hours.
4. Report all *confirmed* and *probable* cases to CDES. Complete the *Haemophilus influenzae* case report form (*www.doh.wa.gov/notify/forms/haem_inf.doc*) and enter the data into the Public Health Issues Management System (PHIMS). Note that ***all*** cases of invasive *H. influenzae* disease in children under 5 years old are reportable regardless of serotype.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Prior to routine vaccination, *H. influenzae* serotype b (Hib) was the most common cause of bacterial meningitis and was a major cause of other invasive bacterial disease (including epiglottitis) in young American children. Prior to the introduction of effective conjugate vaccines in 1988, one child in 200 developed *Haemophilus* disease by the age of five. From 1989 to 2000 there was a 99% reduction in Hib invasive disease among children younger than 5 years of age. The average incidence of Hib in this age group between 2000 to 2004 was 0.14 cases per 100,000. Data from active surveillance sites suggest an expected rate of invasive disease due to non-type-b *H. influenzae* to be 0.9 per 100,000 children younger than 5. This rate can be used as a surveillance indicator for monitoring the completeness of invasive *H. influenzae* case reporting.

A. Etiologic Agent

Haemophilus influenzae is a small, gram-negative coccobacillus bacterium. There are at least six serotypes of *H. influenzae* (designated types a–f) distinguished by their capsular antigens, as well as unencapsulated (nontypable) strains. *H. influenzae* serotype b (Hib) was responsible for 95% of invasive *H. influenzae* infections among children younger than 5 years of age in the prevaccine era. Meningitis occurred in approximately two thirds of children with invasive Hib disease resulting in hearing impairment or severe permanent neurologic sequelae in 15–30% of survivors. Approximately 4% of all cases were fatal.

B. Description of Illness

Invasive disease caused by *H. influenzae* can affect many organ systems. Meningitis is the most common clinical manifestation of invasive Hib disease. Bacteremia, periorbital or other cellulitis, epiglottitis (which may cause life-threatening airway obstruction), septic arthritis, osteomyelitis, pericarditis and pneumonia are other manifestations of invasive *H. influenzae* disease. Onset of symptoms is usually abrupt, and may include fever, headache, lethargy, anorexia, nausea, vomiting, irritability or laryngeal stridor, depending on the system involved. Progressive stupor or coma is common with meningitis.

Infections spread via the bloodstream after penetration of the mucous membranes of the nasopharynx. The exact mechanism allowing the penetration is unknown, but a history of recent upper respiratory tract infection may facilitate invasion. Having had a recent cochlear implant procedure also has been identified as a possible risk factor for invasive disease.

In the prevaccine era, Hib could be isolated from the nasopharynx of 0.5%-3% of normal infants and children but was not commonly found in adults. *H. influenzae* organisms colonize the nasopharynx and may be transient or remain for months in the absence of symptoms (asymptomatic carriage). Thus, isolates from sputum or other non-sterile sites are *not* indicative of invasive disease.

Non-invasive upper respiratory tract diseases, including otitis media, sinusitis, and bronchitis, are often caused by other, nonencapsulated strains of *H. influenzae*. Asymptomatic carriage of these organisms can be extremely common, especially the non-typeable strains, and can be recovered from the nasopharynx of 40 to 80% of children.

C. *Haemophilus influenzae* in Washington State

Invasive disease is markedly age dependent, with peak rates at age 6–18 months. Since the widespread adoption of routine childhood immunization against Hib in 1990, the rates of invasive Hib have fallen dramatically. DOH has received 4 to 13 reports of pediatric *H. influenzae* infections of all types per year recently, with rare fatalities, as compared to 319 reports of invasive Hib disease in 1986, most in young children, with 11 deaths.

D. Reservoir

Humans (cases and carriers)

E. Modes of Transmission

H. influenzae organisms are transmitted person to person by inhalation of respiratory droplets or by direct contact with respiratory tract secretions. Unimmunized children less than 4 years old are considered to be at increased risk of invasive Hib disease, especially if they have had prolonged close contact with a child with invasive Hib disease. Other predisposing factors are conditions such as sickle cell anemia and HIV infection that lead to compromise of the immune system. The risk of secondary disease among household contacts is age dependent and estimated to be 4% for children less than 2 years of age, 1.5% for children 2 to 3 years of age, 0.1% for children 4–5 years of age, and 0% among immunocompetent contacts over the age of 6. The overall risk of secondary disease in the child care setting seems to be less than that in households.

F. Incubation Period

Because persons who acquire *H. influenzae* infections are often asymptomatically colonized, the incubation period is unknown but is probably short, possibly 2–4 days. Most secondary cases in households occur during the first week after hospitalization of the index case although some secondary cases occur later.

G. Period of Communicability

The exact period of communicability is unknown. A person is communicable as long as the organism is present in discharges from the nose or throat which may be a prolonged period, even without active nasal discharge. Communicability ends within 24–48 hours after initiation of appropriate chemoprophylaxis. Note, however, that treatment of invasive disease does not necessarily eradicate the organism from the nasopharynx. Chemoprophylaxis for the purpose of eliminating nasopharyngeal carriage should be given to the index case with invasive Hib disease just before discharge from the hospital if younger than two years of age or a member of a household with a susceptible contact and if treated for invasive disease with a regimen other than cefotaxime or ceftriaxone.

H. Treatment

Initial therapy for children with meningitis potentially caused by Hib includes cefotaxime or ceftriaxone. Alternative therapies are meropenem or the combination of ampicillin and chloramphenicol administered intravenously. For antimicrobial treatment of epiglottitis, arthritis, and other invasive *H. influenzae* infections, including infections caused by strains other than type b, recommendations are similar. Duration of therapy is usually a minimum of 10 days; longer duration of therapy may be indicated in complicated cases.

3. CASE DEFINITIONS

A. Clinical Description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglottitis, or pneumonia.

B. Laboratory Criteria for Diagnosis

Isolation of *H. influenzae* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

C. Case Definition (1997)

Probable: a clinically compatible case with detection of *H. influenzae* serotype b antigen in CSF

Confirmed: a clinically compatible case that is laboratory confirmed

D. Comment

In Washington, only cases under 5 years of age must be reported. Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease. Because antigen detections tests can be positive in urine and serum of person without invasive Hib disease, a case that is identified exclusively by positive antigen tests in urine or serum should not be reported as a true case, but can be considered a suspect case if clinical symptoms are compatible with invasive bacterial disease.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Confirming the diagnosis of invasive *H. influenzae* disease requires culturing *H. influenzae* from a body site which is normally sterile (e.g., CSF, blood, joint fluid, pleural effusion, pericardial effusion, peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid). ALL *H. influenzae* isolates from normally sterile sites in children under 5 years old should be serotyped and tested for antimicrobial susceptibility.

B. Tests Available at Washington State Public Health Laboratories (PHL)

PHL can provide isolate confirmation and serotyping for *H. influenzae*. Clinical laboratories should be contacted for each reported case to assure that all pediatric *H. influenzae* isolates are forwarded to the PHL.

C. Specimen Collection

Isolates should be submitted to PHL on media that support its growth. In the event of an outbreak, contact CDES for assistance in determining which additional specimens should be collected for laboratory study. Include the microbiology forms with all specimens: http://www.doh.wa.gov/EHSPHL/PHL/Forms/Microbiology.pdf

5. ROUTINE CASE INVESTIGATION

A. Evaluate the Diagnosis

Review the clinical presentation, risk factors for exposure, and immunization status of the patient. Assure that laboratories submit all *H. influenzae* isolates obtained from a sterile

site from children under 5 years old to Public Health Laboratories for confirmation and serotyping.

B. Identify Source of Infection

Usually, identification of the source of infection is not possible because asymptomatic persons can carry the organism in their nose and throat. It is important to verify whether any household or child care contacts have had any illness suggestive of *H. influenzae*-caused invasive disease within the previous 60 days.

C. Identify Potentially Exposed Persons

While awaiting the serotype result:

1. Identify young children (under the age of 5) who are household or childcare contacts of patients and assess their immunization status. This will help identify persons who should receive antimicrobial prophylaxis if Hib disease is confirmed, or who should be immunized (see Section 6).
2. Determine whether the case had prolonged contact with other children under 2 years of age in a child care setting in the week prior to onset of illness. If so, refer to Section 7. Secondary transmission in child care centers is rare if all the contacts of the case are older than 2 years of age.

   See recommendation for contact management in Section 6 if the serotype is determined to be type b.

D. Environmental Evaluation — None

6. CONTROLLING FURTHER SPREAD

The following recommendations to control further spread pertain only to cases of *H. influenzae* invasive disease due to serotype B (Hib).

A. Infection Control Recommendations / Case Management

1. Children with known or suspected *H. influenzae* serotype b (Hib) disease should be cared for using droplet precautions until 24 hours after initiation of appropriate antibiotic therapy.
2. Children with Hib disease who are younger than 2 years or who have a susceptible household contact should receive appropriate treatment to eliminate respiratory carriage for at least 24 hours before resuming contact with any susceptible persons. Treatment of Hib invasive disease with ceftriaxone or cefotaxime will also eradicate nasal carriage. Treatment with meropenem, ampicillin or chloramphenical does not eradicate carriage, thus, children receiving these antibiotics should be treated with rifampin.
3. Children developing Hib invasive disease before the age of 2 years are at increased risk of recurrent Hib disease. They should be immunized according to an age-appropriate schedule initiated as soon as possible during convalescence. Any earlier doses of Hib vaccine received by such children should be discounted.

B. Contact Management

1. Education

If children under 4 years old are potentially exposed to a patient with Hib disease, their parents or guardians should be instructed to monitor their children for signs of illness (e.g., fever, lethargy, irritability, loss of appetite, vomiting), and to seek medical care immediately should any illness occur. Most secondary cases in households occur during the first week after hospitalization of the index case although some secondary cases occur later.

2. Antibiotic Prophylaxis

Chemoprophylaxis with rifampin is recommended for *all* members of the immediate household of Hib cases when the household includes members that meet any of the following:

- A child under age 4 years who is not fully immunized [defined as at least one dose of conjugate vaccine at 15 months of age (or older), or 2 doses at 12–14 months, or a 2- or 3-dose primary series at <12 months with a booster dose at >12 months.]
- An infant less than 12 months of age who has not completed the primary Hib series.
- An immunocompromised child regardless of this child's Hib immunization status.

In general, chemoprophylaxis is not recommended for contacts of a single case of Hib in a child care center.

Chemoprophylaxis is not recommended for contacts of patients with invasive disease caused by non-type b strains of *H. influenzae*.

The rifampin dosage is 20 mg/kg (maximum 600 mg) once daily for 4 days. For neonates (<1 month), the dose is 10 mg/kg once daily for 4 days. Rifampin is available in 150 mg and 300 mg capsules which can be mixed with applesauce, following the manufacturer's instructions. Rifampin chemoprophylaxis is not recommended for pregnant women. Those taking rifampin should be informed that gastrointestinal upset, orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives can occur.

Antibiotic prophylaxis should begin as soon as possible. "Because some secondary cases occur later, initiation of chemoprophylaxis 7 days or more after hospitalization of the index case may be of some benefit (Red Book 2006 p. 314)."

For additional information regarding indications for rifampin chemoprophylaxis for contacts of patients with Hib disease, please see the Red Book 2006 Report of the Committee on Infectious Disease pp. 312–14.

3. Active Immunization

Because of the length of time necessary to develop antibodies, vaccination does not play a major role in the management of contacts. However, unvaccinated or incompletely vaccinated children who are contacts of persons with Hib should receive a dose of Hib vaccine and be scheduled to complete the series.

C. Environmental Measures — None

7. MANAGING SPECIAL SITUATIONS

A. Case Attends Child Care (*H. influenzae* serotype b [Hib] only)

Ascertain if the case was in any child care setting during the week prior to onset. The overall risk of secondary disease in child care settings seems to be less than that in households, and is rare when all child care contacts are older than 2 years.

1. The operator of the facility should be asked about other cases of meningitis or other suspect invasive disease occurring among other children during the past 2 months.
2. The parents of children in the same classroom as the case should be notified (preferably in writing) of the occurrence of Hib disease in the facility. The notice should advise parents to:
    - monitor their children carefully for signs of illness such as fever, irritability, lethargy, and loss of appetite; and
    - seek medical care immediately should such symptoms occur.
3. Instruct the child care operator to notify the local health jurisdiction immediately if another child becomes ill with similar symptoms. When 2 or more cases of Hib have occurred within 60 days and un- or under-immunized children attend the child care facility, rifampin prophylaxis for workers and attendees is generally recommended.
4. Chemoprophylaxis is not recommended for contacts of cases of invasive *H. influenzae* disease due to serotypes other than b.

8. ROUTINE PREVENTION

A. Immunization Recommendations

Haemophilus influenzae serotype b (Hib) vaccine is recommended for all children. The primary series consists of either 3 doses given at 2, 4 and 6 months or 2 doses given at 2 and 4 months depending on the type of vaccine. A booster dose is recommended at 12–15 months of age. Fewer doses are recommended if the series is initiated at an older age.

For more information regarding the types of Hib vaccines and recommended schedules for different Hib vaccines, see: http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm

B. Prevention Recommendations

Vaccination is the best way to protect against invasive disease caused by *Haemophilus influenzae* serotype b.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES